

# What is the Immune System?

<http://www.niaid.nih.gov/topics/immuneSystem/Pages/whatIsImmuneSystem.aspx>

The immune system is a network of cells, tissues, and organs that work together to defend the body against attacks by “foreign” invaders. These are primarily microbes—tiny organisms such as bacteria, parasites, and fungi that can cause infections. It is the immune system’s job to keep them out or, failing that, to seek out and destroy them.

When the immune system hits the wrong target, however, it can unleash a torrent of disorders, including allergic diseases, arthritis, and a form of diabetes. If the immune system is crippled, other kinds of diseases result.

## Self and Nonself

The key to a healthy immune system is its remarkable ability to distinguish between the body’s own cells, recognized as “self,” and foreign cells, or “nonself.” The body’s immune defenses normally coexist peacefully with cells that carry distinctive “self” marker molecules. But when immune defenders encounter foreign cells or organisms carrying markers that say “nonself,” they quickly launch an attack.

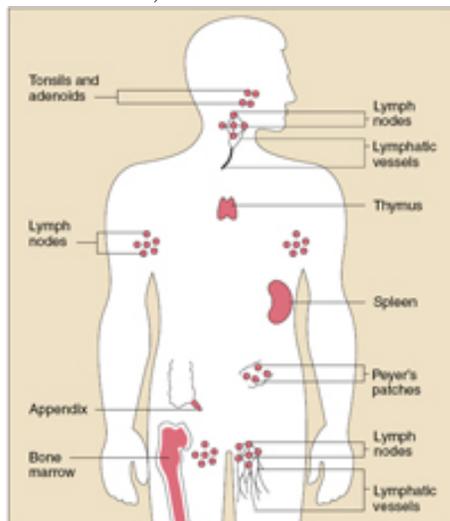
Anything that can trigger this immune response is called an antigen. An antigen can be a microbe such as a virus, or a part of a microbe such as a molecule. Tissues or cells from another person (except an identical twin) also carry nonself markers and act as foreign antigens. This explains why tissue transplants may be rejected.

In abnormal situations, the immune system can mistake self for nonself and launch an attack against the body’s own cells or tissues. The result is called an autoimmune disease. Some forms of arthritis and diabetes are autoimmune diseases.

In other cases, the immune system responds to a seemingly harmless foreign substance such as ragweed pollen. The result is allergy, and this kind of antigen is called an allergen.

## The Structure of the Immune System

Bone marrow, the soft tissue in the hollow center of bones, is the ultimate source of all blood cells, including “lymphocytes” (white blood cells, such as T cells and B cells, which are part of the immune system).



The thymus is a lymphoid organ that lies behind the breastbone. Lymphocytes known as T lymphocytes or T cells (“T” stands for “thymus”) mature in the thymus and then migrate to other tissues.

Lymphocytes can travel throughout the body using the blood vessels. The cells can also travel through a system of lymphatic vessels that closely parallels the body’s veins and arteries.

Cells and fluids are exchanged between blood and lymphatic vessels, enabling the lymphatic system to monitor the body for

invading microbes. The lymphatic vessels carry lymph, a clear fluid that bathes the body's tissues.

Small, bean-shaped lymph nodes are lined along the lymphatic vessels, with clusters in the neck, armpits, abdomen, and groin. Each lymph node contains specialized compartments where immune cells congregate, and where they can encounter antigens.

The spleen is a flattened organ at the upper left of the abdomen. Like the lymph nodes, the spleen contains specialized compartments where immune cells gather and work. The spleen serves as a meeting ground where immune defenses confront antigens.

### **Mounting an Immune Response**

Infections are the most common cause of human disease. They range from the common cold to debilitating conditions like chronic hepatitis to life-threatening diseases such as AIDS. Disease-causing microbes (pathogens) attempting to get into the body must first move past the body's external armor, usually the skin or cells lining the body's internal passageways.

The skin provides an imposing barrier to invading microbes. It is generally penetrable only through cuts or tiny abrasions. The digestive and respiratory tracts—both portals of entry for a number of microbes—also have their own levels of protection. Microbes entering the nose often cause the nasal surfaces to secrete more protective mucus, and attempts to enter the nose or lungs can trigger a sneeze or cough reflex to force microbial invaders out of the respiratory passageways. The stomach contains a strong acid that destroys many pathogens that are swallowed with food.

If microbes survive the body's front-line defenses, they still have to find a way through the walls of the digestive, respiratory, or urogenital passageways to the underlying cells. These passageways are lined with tightly packed epithelial cells covered in a layer of mucus, effectively blocking the transport of many pathogens into deeper cell layers.

Mucosal surfaces also secrete a special class of antibody called IgA, which in many cases is the first type of antibody to encounter an invading microbe. Underneath the epithelial layer a variety of immune cells, including macrophages, B cells, and T cells, lie in wait for any microbe that might bypass the barriers at the surface.

Next, invaders must escape a series of general defenses of the innate immune system, which are ready to attack without regard for specific antigen markers. These include patrolling phagocytes, natural killer T cells, and complement.

Microbes cross the general barriers then confront specific weapons of the adaptive immune system tailored just for them. These specific weapons, which include both antibodies and T cells, are equipped with singular receptor structures that allow them to recognize and interact with their designated targets.

### **B Cells**

B cells and T cells are the main types of lymphocytes. B cells work chiefly by secreting substances called antibodies into the body's fluids. Antibodies ambush foreign antigens circulating in the bloodstream. They are powerless, however, to penetrate cells. The job of attacking target cells—either cells that have been infected by viruses or cells that have been distorted by cancer—is left to T cells or other immune cells (described below).

Each B cell is programmed to make one specific antibody. For example, one B cell will make an antibody that blocks a virus that causes the common cold, while another produces an antibody that attacks a

bacterium that causes pneumonia. When a B cell encounters the kind of antigen that triggers it to become active, it gives rise to many large cells known as plasma cells, which produce antibodies.

## **T Cells**

Unlike B cells, T cells do not recognize free-floating antigens. Rather, their surfaces contain specialized antibody-like receptors that see fragments of antigens on the surfaces of infected or cancerous cells. T cells contribute to immune defenses in two major ways: Some direct and regulate immune responses, whereas others directly attack infected or cancerous cells.

Helper T cells, or Th cells, coordinate immune responses by communicating with other cells. Some stimulate nearby B cells to produce antibodies, others call in microbe-gobbling cells called phagocytes, and still others activate other T cells.

Cytotoxic T lymphocytes (CTLs)—also called killer T cells—perform a different function. These cells directly attack other cells carrying certain foreign or abnormal molecules on their surfaces. CTLs are especially useful for attacking viruses because viruses often hide from other parts of the immune system while they grow inside infected cells. CTLs recognize small fragments of these viruses peeking out from the cell membrane and launch an attack to kill the infected cell.

In most cases, T cells only recognize an antigen if it is carried on the surface of a cell by one of the body's own major histocompatibility complex, or MHC, molecules. MHC molecules are proteins recognized by T cells when they distinguish between self and nonself. A self-MHC molecule provides a recognizable scaffolding to present a foreign antigen to the T cell. In humans, MHC antigens are called human leukocyte antigens, or HLA.

Although MHC molecules are required for T cell responses against foreign invaders, they also create problems during organ transplantations. Virtually every cell in the body is covered with MHC proteins, but each person has a different set of these proteins on his or her cells. If a T cell recognizes a nonself-MHC molecule on another cell, it will destroy the cell. Therefore, doctors must match organ recipients with donors who have the closest MHC makeup. Otherwise the recipient's T cells will likely attack the transplanted organ, leading to graft rejection.

## **Disorders of the Immune System**

### **Allergic Diseases**

The most common types of allergic diseases occur when the immune system responds to a false alarm. In an allergic person, a normally harmless material such as grass pollen, food particles, mold, or house dust mites is mistaken for a threat and attacked.

Allergies such as pollen allergy are related to the antibody known as IgE. Like other antibodies, each IgE antibody is specific; one acts against oak pollen and another against ragweed, for example.

### **Autoimmune Diseases**

Sometimes the immune system's recognition apparatus breaks down, and the body begins to manufacture T cells and antibodies directed against self antigens in its own cells and tissues. As a result, healthy cells and tissues are destroyed, which leaves the person's body unable to perform important functions.

Misguided T cells and autoantibodies, as they are known, contribute to many autoimmune diseases. For instance, T cells that attack certain kinds of cells in the pancreas contribute to a form of diabetes, whereas an autoantibody known as rheumatoid factor is common in people with rheumatoid arthritis. People with

systemic lupus erythematosus (SLE) have antibodies to many types of their own cells and cell components. SLE patients can develop a severe rash, serious kidney inflammation, and disorders of other important tissues and organs.

No one knows exactly what causes an autoimmune disease, but many factors are likely to be involved. These include elements in the environment, such as viruses, certain drugs, and sunlight, all of which may damage or alter normal body cells. Hormones are suspected of playing a role because most autoimmune diseases are far more common in women than in men. Heredity, too, seems to be important. Many people with autoimmune diseases have characteristic types of self-marker molecules.

### **Immune Deficiency Disorders**

When the immune system is missing one or more of its parts, the result is an immune deficiency disorder. These disorders can be inherited, acquired through infection, or produced as a side effect by drugs such as those used to treat people with cancer or those who have received transplants.

Temporary immune deficiencies can develop in the wake of common virus infections, including influenza, infectious mononucleosis, and measles. Immune responses can also be depressed by blood transfusions, surgery, malnutrition, smoking, and stress.

Some children are born with poorly functioning immune systems. Some have flaws in the B cell system and cannot produce antibodies. Others, whose thymus is either missing or small and abnormal, lack T cells. Very rarely, infants are born lacking all of the major immune defenses. This condition is known as severe combined immune deficiency disease or SCID.

AIDS is an immune deficiency disorder caused by a virus (HIV) that infects immune cells. HIV can destroy or disable vital T cells, paving the way for a variety of immunologic shortcomings. The virus also can hide out for long periods in immune cells. As the immune defenses falter, a person develops AIDS and falls prey to unusual, often life-threatening infections and rare cancers.